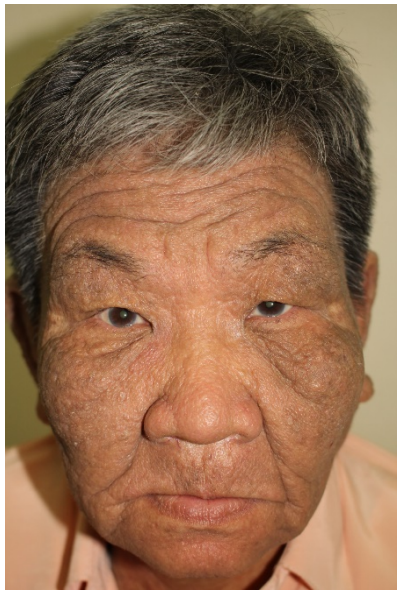
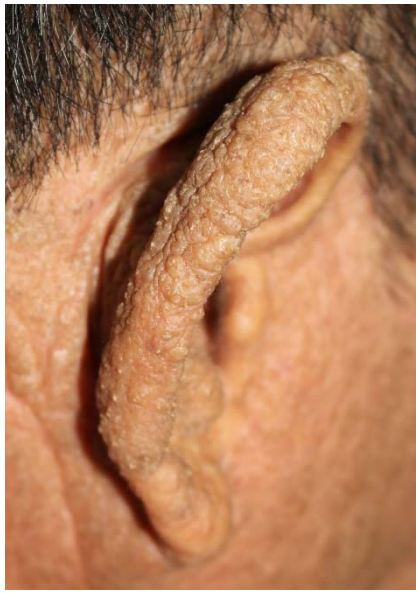
Case 13
A 65 year-old Thai woman
Chief complaint: Progressive multiple pruritic skin lesions

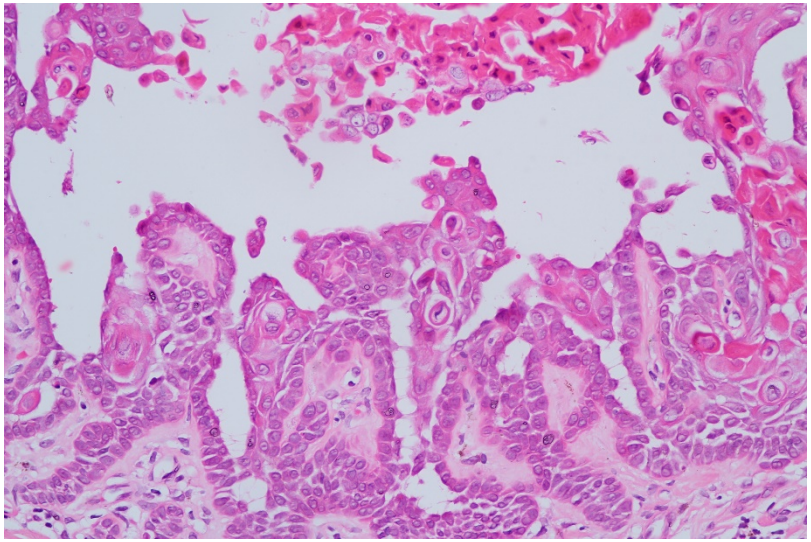
Present illness: The patient presented with progressive multiple pruritic skin-colored plaques on face and upper trunk since she was teenage. The lesions worsened by sunlight, heat and sweating. She had not received any previous treatment.

Past history:
Hypertension

Family history:
She denied family history of similar cutaneous lesions
Skin examination:

- Multiple, ill-defined, skin-colored to yellowish-brown hyperkeratotic papules, some coalescing into plaques were observed on face, both ears, upper chest and back.
- Multiple flat-topped papules on both dorsal hands
- Multiple, ill-defined, painless whitish papules with cobble stone appearance on hard palate.
- Alternating longitudinal erythroleukonychia, longitudinal ridging and brittle nail with V-shaped notches were observed.

Histopathology: (S16-5856A, left ear)



- Hyperkeratosis, hypergranulosis and papillated epidermal hyperplasia
- Multiple discrete zones of suprabasal clefts with acanthosis dyskeratotic cells in the spinous and granular layer ("corps ronds") and parakeratotic cornified layer ("grains") or focal acanthotic dyskeratosis (FAD)

Diagnosis: Darier's disease
Treatment:

- Genetic counselling
- Reduce exacerbations: avoid heat, sweating, UVB
- 10% Urea cream apply body bid.
- 5% Lactic acid apply lesion 15-30 min then washout bid.

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Discussion:

Darier's disease (dyskeratosis follicularis; DD) is a relatively rare autosomal dominant disease. It was first described independently by Darier and White in 1889. Darier's disease has been reported in both sexes and all ethnicities.[1] The prevalence is reported from 1/30,000 to 1/100,000.[1, 2] The onset ranges from 6 to 20 years of age. Despite the inheritance pattern of the disease, 47% of the patients do not have any family history.[3]

The characteristic lesions present as yellowish-brown hyperkeratotic papules coalescing into plaques in seborrheic areas such as forehead, central chest, back and scalp margins. Malador and pruritus are typical features.[4] It is worsened by sunlight, mechanical trauma, heat, humidity and infection. In some female cases, menstrual period aggravates symptoms. Associated findings include nail abnormalities characterized by red and white longitudinal bands and distal v-shaped notches of the nail plate. Other symptoms include white papules on oral mucosa (cobblestoning), pitted keratosis on palms and soles and skin-colored flat topped papules on the dorsal of hand and/or feet. Neuropsychiatric disease including seizures, bipolar disorder and schizophrenia has been reported in association with Darier's disease.[5]

The etiology of Darier's disease is mutation in the ATP2 A2 gene. The gene encoding sarco/endoplasmic reticulum ATPase type 2 (SERCA 2) which maintains high calcium concentrations in the lumen.[5] Lowering Ca^{2+}concentration in the ER leads to ER stress responses and cell apoptosis.[5, 6]

Clinical subtypes are divided into generalized and segmental types. Type 1 segmental Darier's disease results from a postzygotic mutation in the ATP2A2 gene during embryogenesis, which leads to a mosaic pattern on normal skin. In contrast, type 2 segmental patients have more severe mosaic patterns on a background of generalized Darier's disease as a result of postzygotic inactivating mutation in patients who had germline mutation.[6]

Major histologic features are acantholysis and dyskeratosis. Acantholysis is caused by loss of cell adhesion and leads to suprabasal cleft formation. Dyskeratosis is due to apoptosis of keratinocytes. These dyskeratotic cells are describes as "corps ronds" in malpighian layer and "grains" in statum corneum.[3] The overlying epidermis shows hyperkeratosis and papillomatosis. Histopathology in Grover's disease resembles that of Darier's disease, but there tends to be more acatholysis and less dyskeratotic cells.

Treatment remains a major challenge. Currently, there is no validated curative treatment. In general, genetic counselling and lifestyle advice are important. Cool cotton clothing and sunscreen help prevent aggravation due to heat, sweating and sun exposure.[4] Topical retinoids such as isotretinoin[7], adapalene[8] and tazarotene[9] have been reported to reduce hyperkeratosis, but cause irritation. Using topical retinoid in combination with emollients or mid-potency topical steroid reduces pruritus.[4] Other topical treatments reported include topical 5-fluorouracil,[10] 3% diclofenac gel[8] and calcipotriol ointment. Oral retinoids are effective,[4] however, dose-related side effects are common. Surgical treatment has been recommended for hypertrophic disease.[4, 11] Additionally, laser ablation including carbon dioxide, Er:YAG and pulsed-dye lasers were reported to

have benefits in recalcitrant plaques.[12, 13]

References

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